

This listing of claims will replace all prior versions, and listings, of claims in the application:

In the Claims

Claims 1-35 (Cancelled)

36. (currently amended): A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and one or more heterologous transcriptionally active elements incorporated 3' with respect to the ITR, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the one or more heterologous transcriptionally active elements under conditions permissive for transcription, wherein at least one of the one or more heterologous transcriptionally active elements is a **human transcriptionally active element from a human gene**, and wherein the region is less than about 400 **bp nucleotides** in length.

37. (currently amended): A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 200 **bp nucleotides**.

38. (previously presented): A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about seven-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

39. (previously presented): A polynucleotide according to claim 38 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a transcription initiator sequence and at least one CCAC box.

40. (currently amended): A polynucleotide according to claim 39 wherein the transcription initiator sequence and at least one CCAC box are contained within a polynucleotide segment less than about 90 **nt nucleotides**.

41. (previously presented): A polynucleotide according to claim 40 wherein the one or more transcriptionally active elements have at least about 90% overall identity to SEQ ID NO:17, or the sequence complementary thereto.

42. (previously presented): A polynucleotide according to claim 39 wherein said polynucleotide comprises SEQ ID NO:17.

43. (previously presented): A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 10-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

44. (currently amended): A polynucleotide according to claim 43 36 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a transcriptionally active element of an amyloid β -protein precursor (APP) promoter and a transcription initiator sequence.

45. (currently amended): A polynucleotide according to claim 44 wherein the transcriptionally active element of an amyloid β -protein precursor (APP) promoter and the transcription initiator sequence are contained within a polynucleotide segment less than about 70 ~~nt~~ nucleotides.

46. (previously presented): A polynucleotide according to claim 45 wherein the transcriptionally active element has at least about 90% overall sequence identity to SEQ ID NO:7, or the sequence complementary thereto.

47. (previously presented): A polynucleotide according to claim 44 wherein said polynucleotide comprises SEQ ID NO:7.

48. (previously presented): A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 40-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

49. (previously presented): A polynucleotide according to claim 36 wherein the transcriptional activity is increased at least about 50-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription.

50. (previously presented): A polynucleotide according to claim 36 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

51. (previously presented): A polynucleotide of claim 50, wherein the gene is a CFTR gene.

52. (previously presented): A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific, and wherein the heterologous segment has a deletion compared to its native sequence.

53. (previously presented): A polynucleotide according to claim 52 wherein the heterologous segment is less than 200 nucleotides.

54. (previously presented): A polynucleotide according to claim 52 wherein the heterologous segment is less than 100 nucleotides.

55. (previously presented): A polynucleotide according to claim 52 wherein at least one of the transcriptionally active elements is tissue specific.

56. (previously presented): A polynucleotide according to claim 52 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

57. (previously presented): A polynucleotide of claim 56, wherein the gene is a CFTR gene.

58. (previously presented): A polynucleotide comprising a region containing an Adeno-associated virus (AAV) inverted terminal repeat (ITR) and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements which are removed from a promoter, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, and wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific.

59. (previously presented): A polynucleotide according to claim 58 wherein the heterologous segment is less than 200 nucleotides.

60. (previously presented): A polynucleotide according to claim 58 wherein the heterologous segment is less than 100 nucleotides.

61. (previously presented): A polynucleotide according to claim 58 wherein at least one of the transcriptionally active elements is tissue specific.

62. (previously presented): A polynucleotide according to claim 58 further comprising a gene operably linked to the region containing the ITR and transcriptionally active elements.

63. (previously presented): A polynucleotide of claim 62, wherein the gene is a CFTR gene.

64. (currently amended): A polynucleotide comprising, in order:
a region containing a first AAV ITR and one or more heterologous transcriptionally active elements incorporated 3' with respect to the ITR, wherein the transcriptional activity is increased at least about two-fold relative to a polynucleotide containing the ITR and lacking the one or more transcriptionally active elements under conditions permissive for transcription, wherein at least one of the one or more heterologous transcriptionally active elements is a human transcriptionally active element from a human gene, and wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 400 bp nucleotides in length; and
a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

65. (currently amended): A polynucleotide according to claim 64 wherein the region containing the ITR and the one or more transcriptionally active elements is less than about 200 bp nucleotides.

66. (previously presented): A polynucleotide according to claim 64 further comprising a gene operably linked to the region containing the ITR and the one or more heterologous transcriptionally active elements.

67. (previously presented): A polynucleotide according to claim 66, wherein the gene is a CFTR gene.

68. (previously presented): A plasmid comprising a polynucleotide of claim 64, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

69. (previously presented): An AAV viral particle comprising a polynucleotide of claim 64.

70. (currently amended): An AAV viral particle according to claim 69, wherein the polynucleotide is between 4.6 kb 4600 nucleotides and 5.0 kb 5000 nucleotides in length.

71. (previously presented): A polynucleotide comprising, in order:
a region containing a first AAV ITR and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements, wherein the transcriptional activity is increased at least two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific, and wherein the heterologous segment has a deletion compared to its native sequence; and

a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

72. (currently amended): A polynucleotide of claim 71, wherein the starting site of the first AAV ITR and the ending site of the second AAV ITR are contained within a polynucleotide segment between 4.6 kb 4600 nucleotides and 5.0 kb 5000 nucleotides in length.

73. (previously presented): A polynucleotide of claim 71, wherein the heterologous segment is less than 200 nucleotides.

74. (previously presented): A polynucleotide of claim 71, wherein at least one of the transcriptionally active elements is tissue specific.

75. (previously presented): A polynucleotide of claim 71, further comprising a gene operably linked to the region containing the ITR and the heterologous segment.

76. (previously presented): A polynucleotide of claim 75, wherein the gene is a CFTR gene.

77. (previously presented): A plasmid comprising a polynucleotide of claim 71, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

78. (previously presented): An AAV viral particle comprising a polynucleotide of claim 71.

79. (currently amended): An AAV viral particle according to claim 78, wherein the polynucleotide is between 4.6 4600 nucleotides and 5.0 kb 5000 nucleotides in length.

80. (previously presented): A polynucleotide comprising, in order:
a region containing a first AAV ITR and a heterologous segment incorporated 3' with respect to the ITR, wherein the heterologous segment comprises one or more transcriptionally active elements which are removed from a promoter, wherein the transcriptional activity is increased at least two-fold relative to a polynucleotide containing the ITR and lacking the heterologous segment under conditions permissive for transcription, and wherein the heterologous segment is less than 500 nucleotides in length and is tissue specific; and

a second AAV ITR selected from the group consisting of a wild-type ITR, a transcriptionally-activated ITR, a D sequence, a trs, or a portion of a wild-type ITR.

81. (currently amended): A polynucleotide of claim 80, wherein the starting site of the first AAV ITR and the ending site of the second AAV ITR are contained within a polynucleotide segment between 4.6 kb 4600 nucleotides and 5.0 kb 5000 nucleotides in length.

82. (previously presented): A polynucleotide of claim 80, wherein the heterologous segment is less than 200 nucleotides.

83. (previously presented): A polynucleotide of claim 80, wherein at least one of the transcriptionally active elements is tissue specific.

84. (previously presented): A polynucleotide of claim 80, further comprising a gene operably linked to the region containing the ITR and the heterologous segment.

85. (previously presented): A polynucleotide of claim 84, wherein the gene is a CFTR gene.

86. (previously presented): A plasmid comprising a polynucleotide of claim 80, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

87. (previously presented): An AAV viral particle comprising a polynucleotide of claim 80.

88. (currently amended): An AAV viral particle according to claim 87, wherein the polynucleotide is between 4.6 4600 nucleotides and 5.0 kb 5000 nucleotides in length.

89. (previously presented): A mammalian cell comprising a polynucleotide according to claim 36, wherein said polynucleotide is stably integrated into a chromosome of said cell.

90. (previously presented): A mammalian cell of claim 89, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

91. (previously presented): A mammalian cell of claim 89, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

92. (previously presented): A mammalian cell comprising a polynucleotide according to claim 52, wherein said polynucleotide is stably integrated into a chromosome of said cell.

93. (previously presented): A mammalian cell of claim 92, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

94. (previously presented): A mammalian cell of claim 92, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

95. (previously presented): A mammalian cell comprising a polynucleotide according to claim 58, wherein said polynucleotide is stably integrated into a chromosome of said cell.

96. (previously presented): A mammalian cell of claim 95, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

97. (previously presented): A mammalian cell of claim 95, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

98. (previously presented): A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a heterologous transcription initiator sequence.

99. (previously presented): A polynucleotide according to claim 36 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a TATA box as a transcription initiator sequence.

100. (new): A polynucleotide according to claim 52 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a heterologous transcription initiator sequence.

101. (new): A polynucleotide according to claim 52 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a TATA box as a transcription initiator sequence.

102. (new): A polynucleotide according to claim 58 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a heterologous transcription initiator sequence.

103. (new): A polynucleotide according to claim 58 wherein the region containing the ITR and the one or more transcriptionally active elements comprises a TATA box as a transcription initiator sequence.

104. (new): A plasmid comprising a polynucleotide of claim 36, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

105. (new): A plasmid comprising a polynucleotide of claim 52, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

106. (new): A plasmid comprising a polynucleotide of claim 58, further comprising an element selected from the group consisting of an origin of replication and a reporter gene.

107. (new): An AAV viral particle comprising a polynucleotide of claim 36.

108. (new): An AAV viral particle according to claim 107, wherein the polynucleotide is between 4600 nucleotides and 5000 nucleotides in length.

109. (new): An AAV viral particle comprising a polynucleotide of claim 52.

110. (new): An AAV viral particle according to claim 109, wherein the polynucleotide is between 4600 nucleotides and 5000 nucleotides in length.

111. (new): An AAV viral particle comprising a polynucleotide of claim 58.

112. (new): An AAV viral particle according to claim 111, wherein the polynucleotide is between 4600 nucleotides and 5000 nucleotides in length.

113. (new): A mammalian cell comprising a polynucleotide according to claim 64, wherein said polynucleotide is stably integrated into a chromosome of said cell.

114. (new): A mammalian cell of claim 113, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

115. (new): A mammalian cell of claim 113, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

116. (new): A mammalian cell comprising a polynucleotide according to claim 71, wherein said polynucleotide is stably integrated into a chromosome of said cell.

117. (new): A mammalian cell of claim 116, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

118. (new): A mammalian cell of claim 116, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.

119. (new): A mammalian cell comprising a polynucleotide according to claim 80, wherein said polynucleotide is stably integrated into a chromosome of said cell.

120. (new): A mammalian cell of claim 119, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene.

121. (new): A mammalian cell of claim 119, wherein said cell comprises an AAV *rep* gene and an AAV *cap* gene stably integrated into a chromosome of said cell.